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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/519,983

01/04/2005

Yasuhiro Kajihara

TAM-051

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KUBOVCIK & KUBOVCIK

SUITE 1105

1215 SOUTH CLARK STREET

ARLINGTON, VA 22202

EXAMINER

BLAND, LAYLA D

ART UNIT

PAPER NUMBER

1623

MAIL DATE

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11/07/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/519,983	Applicant(s) KAJIHARA, YASUHIRO	
	Examiner LAYLA BLAND	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5-7 and 22-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5-7 and 22-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/4/2005, 12/20/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 9, 2008 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed September 9, 2008, and amendment and response to the Final Office Action (mailed December 28, 2007), filed September 9, 2008 wherein claims 1 and 5 are amended, claims 2-4 and 8-21 are canceled, and claims 22 and 23 are newly submitted.

Claims 1, 5-7, 22, and 23 are pending and are examined on the merits herein.

In view of the cancellation of claims 2-4 and 8-21, all rejections made with respect to those claims in the previous office action are withdrawn.

The rejection of claims 1-12 under 35 USC 103(a) as being unpatentable over Wu and Toshiyuki is withdrawn in view of the new ground of rejection presented below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Step (7) of claim 1 is unclear. Step (7) recites "removing the fat-soluble protective group to form a free amino group." The previous step, step (6), does not recite a fat soluble protecting group, and it is unclear which portion of the molecule is being deprotected.

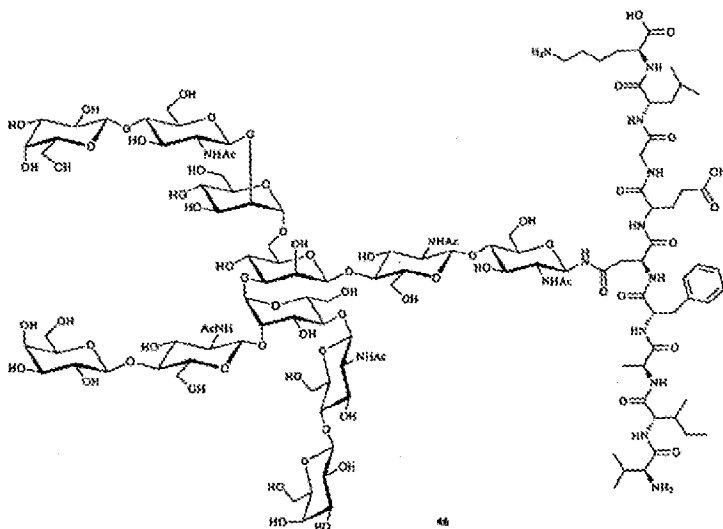
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meinojohanns et al. (J. Chem. Soc. Perkin Trans. I, 1998, pages 549-560, PTO-1449 submitted December 20, 2007) in view of Komba et al. (Journal of Peptide Science, 6: 585-593 (2000), PTO-1449 submitted December 20, 2007).

Meinojohanns et al. teach a method for preparing N-linked glycopeptides such as the one shown below [page 556, Scheme 5]:



The products can be prepared by attaching an Fmoc-protected amino acid to a resin, followed by deprotection of the Fmoc group and coupling of another amino acid, which is repeated. Then the asparagine building blocks, which are protected with Fmoc as well (see page 555, Scheme 4), are coupled and the peptide synthesis is continued as described above. Finally, the glycopeptide is cleaved from the resin. [pages 559-560]. Secreted and cell-surface proteins are glycosylated with both N- and O-linked oligosaccharides, and the effects of the sugars on such properties as immunogenicity is of importance [page 549, first paragraph]. The N-linked glycopeptides prepared by Meinojohanns could be used as substrates for 1-6-sialyltransferase [page 556, scheme 5].

The difference between Meinojohanns' process and the claimed process is that Meinojohanns does not utilize an asparagine-linked oligosaccharide containing a sialyl moiety, but instead suggests the use of sialyltransferase to introduce sialyl moieties.

Komba et al. teach the preparation of Sialyl-T-Glycopeptides (which are O-linked as opposed to Meinojohanns' N-linked glycopeptides). Sialylation is a method of circumventing recognition by the immune system [see abstract]. The products were prepared via the Fmoc/OPfp-ester strategy, as shown below [page 590, Figure 1]:

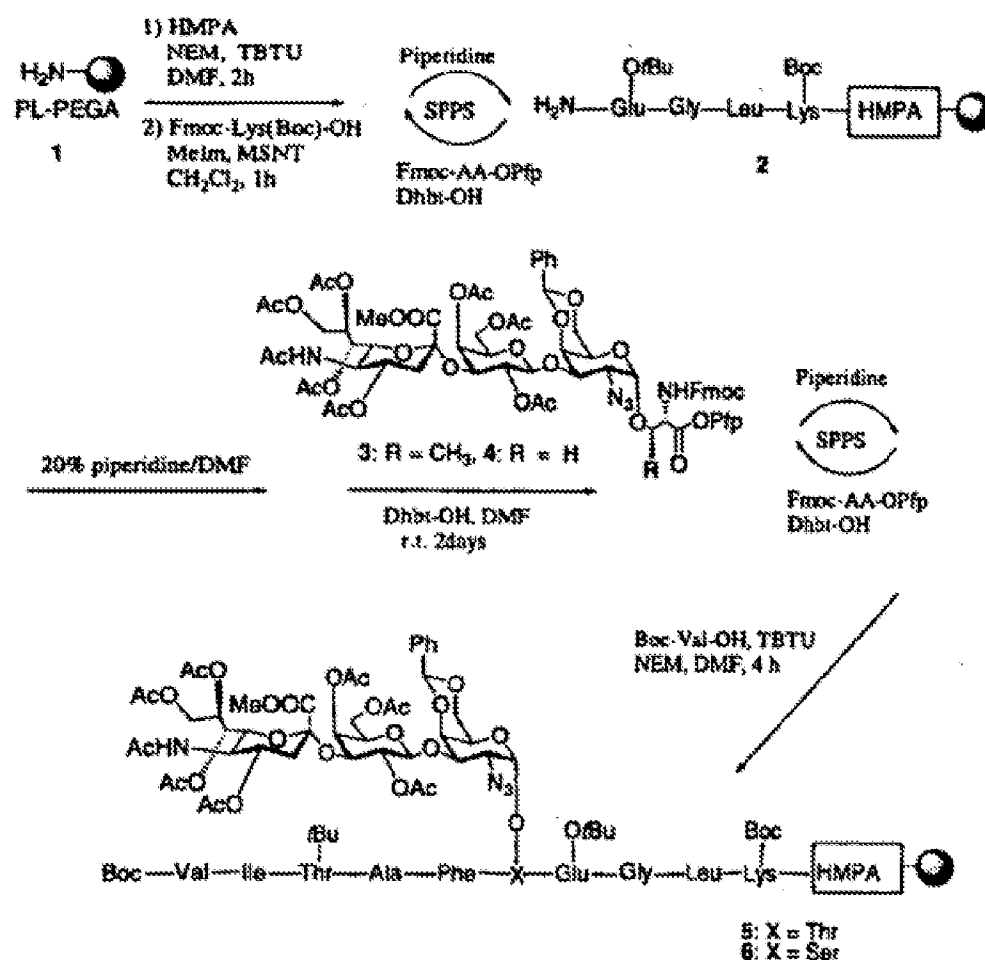


Figure 1 Solid-phase glycopeptide synthesis.

The glycopeptides were cleaved from the resin before deprotection of sialic acid, because the free carboxylic acid on the 1-position of sialic acid rendered the glycosidic linkage more susceptible to cleavage [page 590, first paragraph].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to carry out the method of Meinojohanns using sialylated oligosaccharides. The Supreme Court in KSR reaffirmed the familiar framework for determining obviousness as set forth in *Graham v. John Deere Co.* (383 U.S. 1, 148 USPQ 459 (1966)), but stated that the Federal Circuit had erred by applying the teaching- suggestion-motivation (TSM) test in an overly rigid and formalistic way. KSR, 82 USPQ2d 1385. Exemplary rationales that may support a conclusion of obviousness include:

- Combining prior art elements according to known methods to yield predictable results;
- Simple substitution of one known element for another to obtain predictable results;
- Use of known technique to improve similar devices (methods, or products) in the same way;
Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
- “Obvious to try” – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success.
- Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;
- Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

In this case, use of a known technique to improve a similar method in the same way would lead the skilled artisan to the claimed invention. The claimed invention can be seen as an improvement over the method of Meinojohanns because the sialyl group is present without requiring additional enzymatic transformation. However, Komba teaches a method wherein the sialyl moiety can be introduced chemically, attached to the oligosaccharide, via protection of the acid group. One of ordinary skill in the art

could have applied Komba's technique to Meinojohanns' method and would have expected the modification to be successful, because the two methods are otherwise quite similar.

Using a different rationale, there was a teaching in the Meinojohanns reference that suggested the use of sialyltransferase, a teaching in the Komba reference regarding the importance of sialyl groups in glycopeptides, and a teaching of how to prepare sialylated glycopeptides. Thus, the skilled artisan would be motivated to prepare sialylated derivatives of the Meinojohanns glycopeptides, and could use the Komba method to do so.

Claims 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meinojohanns et al. (J. Chem. Soc. Perkin Trans. I, 1998, pages 549-560, PTO-1449 submitted December 20, 2007) in view of Komba et al. (Journal of Peptide Science, 6: 585-593 (2000), PTO-1449 submitted December 20, 2007) as applied to claims 1 and 5-7 above, and further in view of Ratcliffe et al. (US 5,527,901, June 18, 1996).

Meinojohanns et al. and Komba et al. teach as set forth above, a method utilizing oligosaccharides wherein the sialyl group is protected as the methyl ester, but do not teach the use of oligosaccharides wherein the sialyl group is protected as a benzyl ester.

Ratcliffe et al. teach a method for preparing sialic acid glycosides. Sialic acid glycosides occur in complex oligosaccharides attached to proteins [column 1, lines 57-59]. Synthetic strategies for higher sialosides typically use a methyl ester as a blocking

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group for the acid moiety, but the use of methyl ester results in limitation of subsequent use of the product, because it is difficult to deblock the sialoside while maintaining other ester groups [column 2, line 55 – column 3, line 5]. Benzyl or phenacyl ester blocking groups give a higher yield of product and higher anomeric purity [column 4, lines 1-7].

It would have been obvious to one of ordinary skill in the art to carry out the method, as described above, but using benzyl protection in place of methyl protection for the carboxyl group of sialic acid. Komba et al. teach the use of the methyl ester. Ratcliffe et al. teach that the benzyl ester is an alternative to the methyl ester for protection of the carboxyl group of sialic acid, and offers benefits such as more effective removal in the presence of other blocking groups, higher yields, and higher anomeric purity. Thus, the skilled artisan could have employed the benzyl ester in the method as described above, and would have expected the method to be successful.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/Layla Bland/
Examiner, Art Unit 1623